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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,595	07/05/2000	Leena Peltonen	VOSS1130	1041

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Lisa A Haile
Gray Cary Ware & Freidenrich
Suite 1600
4365 Executive Drive
San Diego, CA 92121

EXAMINER	
LIU, SAMUEL W	
ART UNIT	PAPER NUMBER
1653	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,595	PELTONEN ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3 February 2003 and 8 March 2000.* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-62* is/are pending in the application.

4a) Of the above claim(s) *49-53 and 55-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-48,54 and 62* is/are rejected.

7)☒ Claim(s) *29, 34 and 44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DTAILED ACTION

Applicant's preliminary amendment as to cancellation of claims 1-28 and addition of claims 29-61 filed 8 March 2000 (Paper No. 5), amendment filed 3 February 2003 (Paper No. 18) as to amendment of claims 29 and addition of claims 62, and Applicant's requests for extension of time of three months filed 3 February 2003 (Paper No. 17) and extension of time of five months filed 25 January (Paper No. 10) have been entered.

Foreign Priority

Applicants' claim for foreign priority under 35 U.S.C. 119 (a)-(d) is acknowledged. The copies of the Germany 97 17154.1, 97 117398.4 and 97 119810.6 have been received and considered.

Election/Restrictions

Applicant's election of Group I, claims 29-48 and 53 with additional election of (i) and a polynucleotide (SEQ ID NO:1) encoding polypeptide of SEQ ID NO:2 and (ii) isolated cells as a host for the examination filed 3 February 2003 with traverse without (Paper No. 18) is acknowledged. The traversal is on the ground that all polynucleotide sequences set forth in claim 29 and dependent claims should be examined together because they share commonality of operation, function, or effect (se page 3, the last two paragraphs). The Applicant's traversal has been considered and is persuasive on the basis of the statement in the response (page 4, the first full sentence) which indicates the "...species are not patentably distinct...".. Also, Applicant's request for prosecution of new claim 62 (see page 4) is considered.

Thus, the pending claims 49-53 and 55-61 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected inventions. Claims 29-48, 54 and 62 are examined in this Office action.

Objection to Specification/claims

The disclosure is objected to because of the following informalities:

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

In page 2, line 14, "HLA" should be spelled out for the first instance of use. See also page 5, line 9, "TIF1" and the last fifth line from the bottom, "SSC", "SDS" and ssDNA"; page 8, the third line from the bottom, "PHD"; page 14, line 8, "GST", GFP" and "HA"; page 17, line 5, "ELISA" and RIA"; and page 35, line 10, "RT-PCR".

In page 23, line 1 under Figure 18 section, there appears missing a word or phrase between "human" and "in a series…".

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable codes in page 19, line 14 and page 26, line 6, the forth paragraph. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

In claim 29, an article "a" should be inserted between "in" and "mutated".

Claim 34 is objected to as noncompliant with 37 CFR 1.821 (d). Figure 14 contains a sequence but the claim has no requisite "SEQ ID NO:_". Please note that there is no *per se* Fig 14, but only 14A, 14B and 14C.

Claim 44 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only--, and/or, --cannot depend from any other multiple dependent claim, e.g., claim 42. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 29-48, 54 and 62 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claim 29 and dependent claims thereof, as written, do not sufficiently distinguish over other polynucleotide, polypeptide, proteins, cells and antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate

the hand of the inventor, *e.g.*, by insertion of "Isolated" or "Purified" as disclosed on pages 23-24 and page 34 (isolation of the mouse AIRE gene) of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-48 and 54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of the polynucleotide of SEQ ID NO:1 and a method of producing a polypeptide comprising the polynucleotide (claim 48). Applicant is not in possession of any isolated polynucleotides of SEQ ID NO:1; or any the nucleotide sequences that are only a portion of the full-length of SEQ ID NO:1 sequence or any sub-sequences comprising more than 14 (i.e., "at least about 14") consecutive nucleotides derived from SEQ ID NO:1, including naturally or recombinantly-generated (*in vivo* or *in vitro* mutated) molecules thereof.

The current claim language encompasses a large number of the polynucleotide variants that are both structurally and functionally deviated from the claimed full-length APECED polynucleotide of SEQ ID NO:1. The specification provides insufficient teaching, guidance, and no working examples as to make and use of the variant molecules in formulating the claimed pharmaceutical composition (see claim 54).

The specification does not provide an animal model to demonstrate using the claimed composition and there is apparent indicating relevant animal model for the composition either; thus, applicants are not in possession of the pharmaceutical composition comprising the polynucleotide and variants thereof.

Because the specification is silent in description or/and working examples as to what is a loss of function or a gain of function (see claim 35), applicants are not in possession of any mutant polynucleotide molecules with respect to the biological function(s) of the APECED encoded protein.

The claims of the instant application recite that the polypeptide encoded by APECED polynucleotide has the function of a transcription factor or transcription-associated factor (see claim 30). Yet, there are insufficient teaching, guidance or/and working examples in this regard. Thus, applicants are not in possession of the polypeptide(s) encoded by the polynucleotide or sub-subsequence thereof which have the transcription factor activity or transcription-associated factor activity.

Also, the claims recite a "mammalian homologue" of the claimed polynucleotide (see claim 32). Note that the homologue represents a genus encompassing numerous analogs or derivatives of the claimed polynucleotides. The specification, however, provides insufficient description in this regard. Thus, applicants are not in possession of any polynucleotide sequences homologue to human polynucleotide of SEQ ID NO:1 from all mammals. The factual sequence data in regard to the homology in respect to the SEQ ID NO:1 is needed for enablement.

Applicant has disclosed only the polynucleotide of SEQ ID NO:1; therefore, the skilled artisan cannot envision all the contemplated nucleotide sequence possibilities recited in the

instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993).

Making changes from sub-sequence comprising from 14 nucleotides (or a portion) to the full-length SEQ ID NO:1 sequence does not provide maintaining the same three-dimensional structure of the polypeptide encoded by the polynucleotide as by the 100% identity over that of the full-length SEQ ID NO:1. The claim language of claims 29 and 35 appears to encompass all possible mutations *e.g.*, insertion, deletion, substitution and inversion, which can be produced either *via in vitro* mutagenesis or *via* genetics, without regarding structure-function relationship. This would create numerous variants/mutants that are unpredictable. Note that the claim language broadly encompasses a variety of human-generated (i.e., recombinant) mutations apart from those genetically generated. Applicants therefore are not possession of having all types of mutations of the claimed polynucleotide generated *via* protein engineering or other mutagenesis approaches. Without characterization each polynucleotide mutant, the encoded polypeptide mutant thereof is unpredictable in view of structure and function. Because the specification fails to describe the consequence of the mutants and the common attributes or characteristics that identify any APECED mutant or establish any animal model regarding the therapeutic use of the mutant molecule for treating the APECED disease state, the specification is thus insufficient to enable skilled artisan to practice the invention as broadly claimed without an undue amount of experimentation. The mutants recited in the present claim language would render the claims so

broad that the scope of claims is outside the bounds of the enablement and would have resulted in the necessity of undue experimentation

Furthermore, the claims of the present invention recite the hybridization condition (see claims 29, 34 and 44) for a polynucleotide without setting forth a particular condition thereof. In light of the fact that possibility of a polynucleotide anneals to the known polynucleotide molecule under undefined hybridization condition would be enormous and unpredictable, quantity of the variants or mutants encompassed by the current claim language would be far beyond what can be predicted.

Description of invention's reduction to practice, unaccompanied by any meaningful, distinguishing characteristics of evolved the polynucleotide mutants or mutants and use of the mutants or variants for formulating the pharmaceutical composition comprising the polynucleotide mutant is insufficient to satisfy written description requirement of 35 U.S.C. §112, since inventors could have provided description of the mutant(s) or variant(s) of SEQ ID NO:1 polynucleotide, especially those produced by *in vitro* protein-engineering or mutagenesis, since actual reduction to practice may demonstrate possession of embodiment of invention, but it does not necessarily describe what invention is, and since, in context of present case, disclosure of manner in which invention was reduced to practice does not satisfy more fundamental written description requirement set forth in Section 112.

The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and or

chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that the applicants were in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of the polynucleotide variants or/and mutants, which are recombinantly but not genetically produced, to describe its use in testing for a carriership for APECED or for a corresponding disease state (see page 1). Thus, Applicant was not in possession of the claimed polynucleotide variants/mutants or sub-sequences of the SEQ ID NO:1 and use of the same to recombinantly produce polypeptides thereof. *See University of California v. Eli Lilly and co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

In consideration of the issued stated *supra*, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC §112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-48, 54 and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is indefinite in "a portion" in item b, because the specification does not sufficiently define the recited portion; does the recitation include oligonucleotides as small as bi-nucleotides or tri-nucleotides? Also, claim 29 recites "hybridizing to"; such the recitation is ambiguous because hybridization condition is largely varied with different characteristics of nucleotide sequences, *e.g.*, length, GC% and secondary structure if any, and the specification does not define the condition. In the absence of a clear definition of the metes and bounds of this phrase it is unclear which conditions are necessary to "hybridizing" and the specificity needed. See also, claims 3 and 44. The dependent claims are also rejected.

Claim 30 recites "function of transcription factor ...", what is the "function" of the factor to which the claim refers? Dose the function refer to that of transcription or some other function of the protein encoded by the polynucleotide molecule?

Claim 31 recites "double-paired zinc finger motifs"; such the recitation is awkward and unclear because the recitation has not been defined in the specification, and the recitation is vague as to whether or not the term "double" modifies "paired" or two sets of "paired zinc finger motifs'.

Claim 34 is indefinite in reference to figure 14 because the application contains no figure 14. There is a figure 14A, 14B, and 14C to which the claim should refer to instead.

Claim 35 recites "deviating"; the recitation does not clearly characterize the claimed polynucleotide of mutation; does the recitation refer to that the molecule resulted from the

mutation scientifically differ from wild-type molecule as function and structure are concerned? Also, claim 35 is unclear as to "and/or"; which is it, "and" or "or"? Further, claim 35 is indefinite in "a loss of function or a gain of function"; what is the function being lost or gained?

Claim 37 is not apparent in "nucleotides 1085-1097" because such the recitation does not make it clear as to whether or not the nucleotides are or are not consecutive in the sequence.

Claim 41 is indefinite because the claims recites "at least about14 nucleotide" and the at least" is a narrower range than "about" which falls outside of this range.

Claim 48 is indefinite because it is multiply dependent from claim (claim 46) which is itself multiply dependent from claims 35 and 29.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 29, 32, 34-35 41, 43, 45-47 and 54 are rejected under 35 U.S.C. 102(e) as being anticipated by Klinger, K. W. et al. (US Pat. No. 6071717).

Klinger et al. disclose a polynucleotide hybridizes to the polynucleotide of the current invention (see SEQ ID NO: 2 of the patent from nucleotides 1535 to 1564 which is complementary to the nucleotide sequence form nucleotides 2089 to 2118 of the SEQ ID NO:1 of the instant disclosure). Thus, Klinger et al. teaching anticipates the application claims 29 (item c, claim 34, item c, and claims 41 and 43.

The Klinger patent is also applied to claim 35 of the instant application because the claim 35 recites "at least one mutation" that includes deletion (see the claim item c), which renders the patent an anticipatory art over the subjection matter of the claim.

The Klinger sequence is obtained from human, which is applied to claim 32 of the instant application.

Klinger et al. teach cloning the polynucleotide (SEQ ID NO:2) into a vector (see the patent claims 1 and 7, and column 19) and a host (see the patent claim 9) that includes bacteria, yeast and animal cells (see column 8, lines 40-55) *etc.*, as applied to the application claims 45-47.

Also, Klinger et al. teach a therapeutic composition comprising the polynucleotide (see column 13 and the patent claim 22), as applied to claim 54 of the instant application.

Claim Rejections - 35 USC §103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as

a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29, 32, 34, 35, 41-48, 54 and 62 are rejected under 35 U.S.C. 103(a) as being obvious over Aaltonen, J. et al. (Genome Res. (August, 1997) 7, 820-829) taken with Bjorses, P. et al. (*Am. J. Hum. Genet.* (1996) 59, 879-886) and Korenberg, J. R. et al. (US Pat. No. 6166180).

Aaltonen et al. teach localization of an autoimmune-polyendocrinophy-candidiasis-ectodermal dystrophy (APCED) gene in a 800 kb region of human chromosome 21q22.3 using fiber fluorescence *in situ* hybridization (FISH), as applied to claims 29 (item c), 32, 34 (item c), 41-43 and 62 of the instant application.

Also, Aaltonen et al. teach primers used for genotyping the APECED gene (see "Methods" section), as applied to claim 44 of the current application.

Bjorses et al. teach localization of an autoimmune-polyendocrinophy-candidiasis-ectodermal dystrophy (APCED) gene in human chromosome 21q22.3 using linkage and haplotype analyses (see abstract and "Families and Methods" section), as applied to claims 29,

32, 34, 41-43 and 62 of the instant application. Also, Bjorses et al. teach that in different populations (*human*) APECED is due to a spectrum of mutation in a gene (see the last sentence of abstract, and page 886), strongly suggesting that APECED represents a novel gene locus, which will have to be isolated by positional cloning" (see page 886, the second to the last sentence); the Bjorses teaching is applied to claim 35 of the current application. Further, Bjorses et al. teach development of the DNA diagnostics of the APECED in the population having APECED phenotype, suggesting a pharmaceutics application of the APECED gene, as applied to claim 54 of the current application.

Neither Aaltonen nor Bjorses explicitly teach vector, host and a method for use of the polynucleotide in production of the encoded polypeptide thereof.

Korenberg et al. teach chromosome 21 gene marker, an isolated polynucleotide in chromosome 21q22.3 region (see column 4, lines 28-47) wherein the APECED gene also resides, and teach a vector comprising the cloned polynucleotide (see column 8, lines 52-65) and a host cell, *e.g.*, mammalian cell, for expression of the polynucleotide (see column 7, lines 15-49). The Korenberg teaching is applied to claims 35 and 44-47.

Korenberg et al. teach that the polynucleotide is subject to substitution mutagenesis (see the bridging columns 7-8), as applied to the application claim 35. Also, Korenberg et al. teach a method for producing a polypeptide encoded by the polynucleotide (see column 7), as applied to the application claim 48.

One of ordinary skill in the art would have combined the teachings of the above references because (*i*) Bjorses et al. localize an APECED gene in human chromosome 21q22.3

region, provide a good basis for isolating the APECED gene and indicate that APECED represents *a novel* gene locus (see the second last sentence, page 886); the is gene is of great interest since it would be the first gene identified for facilitating diagnosing APECED disease state especially in Finnish and Iranian Jewish populations (see page 886), (*ii*) Aaltonen et al. narrow down the region explored by Bjorses *et al.* to a 800 kb segment of the APECED gene, and (*iii*) Korenberg et al. provides teaching as to an expression vector–host system for producing the gene product.

One would have been motivated to combine the above references to successfully arrive the current invention set forth in the claims *supra* as one is inextricably led to the APECED gene sequence since Bjorses et al. has suggested using positional cloning to finally isolate the gene, and, in fact, Aaltonen et al. teach use of the positional cloning (see abstract, and right column, page 825) in combination of FISH method for cloning the APECED cDNA. In order to obtain the gene product, the skilled artisan would also have adapted Korenberg's vector-host system to make the polypeptide encoded by the APECED polynucleotide including mutant(s). Thus, the claimed invention was *prima facie* obvious to make and use at the time it was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483.

The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr.

Christopher Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

SWL

Samuel Wei Liu, Ph.D.

March 24, 2003

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600